In Canada:
A Trial of Chemoprophylaxis in Inactive Tuberculosis

SUMMARY—One thousand five hundred and thirty-six patients with inactive tuberculosis were given a course of preventive treatment consisting of either INH alone or INH and PAS while 840 similar patients served as a control group. Discontinuation of the treatment was frequent and was usually caused by development of complaints which the patients ascribed to the drugs they were taking.

The annual reactivation rate among controls was 4.9 per 1000. During the period of taking drugs the treated group suffered a reactivation rate of 0.7 per 1000 and those who had taken the medication for at least six months suffered a subsequent annual reactivation rate of 1.3 per 1000. The rate for those who discontinued treatment in the first six months was 5.1 per 1000. There were no reactivations in patients who took INH and PAS for over six months. Bacilli from two of the patients with reactivations who were treated for a prolonged period with INH alone showed resistance to this drug.

Chemoprophylaxis of inactive cases is a potent weapon in tuberculosis control; however, it requires thorough motivation and supervision.

A trial of the use of drugs to prevent reactivation in persons with inactive tuberculosis who had never had adequate chemotherapy was carried out by the directors and staffs of 30 of the tuberculosis clinics and outpatient departments in Canada over a five- to six-year period.[1] The first part of the study was published in 1966.

The criteria for enrolment of inactive cases in the trial were as follows: 1. Selection by the physician-in-charge of a tuberculosis clinic, indicating the likelihood that the individual would carry through a prolonged program. 2. A documented history of active tuberculosis, not previously treated with antimicrobial drugs or having chemotherapy for less than 90 days; or a positive tuberculin test and a radiograph showing definite scarring at the apices, highly suggestive of past unrecognized adult-type tuberculosis, as found, for example, in mass surveys. 3. A period of at least six months of radiological stability, with repeated negative cultures.

Those selected from inactive cases in attendance at the clinics were rechecked for acceptability, while those who had lapsed in attendance were recalled and given the necessary examinations. The purpose of the project was fully explained to all patients fulfilling the three criteria. Only those who volunteered to co-operate fully, to present themselves frequently for examinations, clinical, radiological and bacteriological, as required, and to take the drugs as prescribed, were then accepted. Finally, the previous radiographs of each patient were reviewed by one of the authors (S.G.) as a check on the inactive status.

Although two sputum examinations immediately before enrolment were first stipulated, this proved impractical, since many of the patients insisted that they had neither cough nor sputum. Fewer than half of either the controls or those treated actually had bacteriological examinations immediately before enrolment.

Allocation to one of two drug groups [INH (isoniazid) alone or INH plus PAS (para-aminosalicylic acid)] or to one of three control groups (those not offered any drugs, those who refused drugs but agreed to participate otherwise, and those who were given a placebo) was dependent on the clinic physician and on the patient's choice. Some of the physicians had a preference for INH alone, some for INH plus PAS, and some preferred to carry their patients as controls, with all the necessary supervision; some had a preference for a 12-month course of drugs and others for a course lasting 18 months.

The participants enrolled for chemoprophylaxis numbered 1536; 879 were initially allocated to INH alone (300 mg. daily) and 657 to INH plus PAS (300 mg. INH and 9 to 12 g. PAS daily). Those enrolled as controls numbered 840 (469 not offered any drugs—group I; 353 who refused drugs—group II; and 18 given placebos—group III).

Visits at the clinics were to be at intervals of three months or more often if indicated.

The percentage distributions of the controls and of those allocated to drugs, by sex, age, extent of disease (minimal, moderately advanced, far advanced, and pulmonary plus extrapulmonary), previous documented active tuberculosis, previous chemotherapy, bacteriological status of previous disease, and duration of inactive intervals in those with previous documented active disease are shown in Table I.

From the Department of Medicine, The University of British Columbia, Vancouver, British Columbia.
This study was supported by Federal Research Grant No. 609-7-96.
*Associate Professor, Department of Medicine, University of British Columbia, Vancouver.
†Toronto, Ont.
Reprint requests to: Dr. Stefan Grzybowski, Department of Medicine, University of British Columbia, Vancouver 8, British Columbia.

STEFAN GRZYBOWSKI, M.D.,* **MARY JANE ASHLEY**, M.D.,† **NEIL E. McKINNON**, M.B.,† **GLORIA PINKUS**, **RUTH PHILIPPS** and **ANN BROWN**,
Vancouver, B.C.

TABLE I.—Comparison Between Treatment and Control Groups

	Control groups	*Chemoprophylaxis groups*
Sex—males	49.7%	48.4%
Median age of patients enrolled	48 years	47 years
Previous documented episode of active disease—FA	16.4%	18.8%
—MA	40.4%	40.3%
—Min.	29.2%	20.2%
—Pulm. + non-pulm.	2.4%	5.0%
Without previous documented episode of active disease	11.6%	15.7%
Previous chemotherapy under 90 days	8.7%	13.5%
No previous chemotherapy	91.3%	86.5%
Bacteriological confirmation for previously documented cases	64.0%	71.4%
Average duration of inactive interval	11.7 years	11.7 years

TABLE II.—Duration of Observation

Period completed (months)	*Controls (840)*		*Chemoprophylaxis (1536)*	
	No.	*%*	*No.*	*%*
Up to 3	812	96.7	1512	98.4
6	809	96.3	1506	98.0
12	797	94.8	1468	95.6
18	769	91.4	1406	91.6
24	743	88.3	1298	84.6
36	544	64.7	905	59.0
48	340	40.4	460	30.0
60	131	15.6	195	12.7

TABLE IV.—Period Taking Drugs

Period of taking drugs completed (months)	*INH* (1017)*		*INH + PAS† (519)*		*Total (1536)*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Up to 3	845	83.2	407	78.4	1252	81.6
6	770	75.8	371	71.5	1141	74.3
12	653	64.3	328	63.2	981	63.9
18	233	22.9	226	43.5	459	29.9
over 18	21	2.1	23	4.4	44	2.9

*Includes 138 patients initially placed on INH + PAS who within four months had discontinued PAS but carried on with INH alone.

†Includes 83 patients who took INH + PAS for periods exceeding four months and then carried on with INH alone.

The two groups are remarkably similar; small disparities, such as a slightly greater percentage of those with far advanced disease and those who were previously bacteriologically positive, suggest that the drug groups might be more susceptible to reactivation than the controls, but the difference would not be great.

OBSERVATIONS

Duration of Observation

Table II shows the periods of observation completed for the controls and for those given drugs. Of the dropouts (3 to 4%) in the first six months, most occurred in the first month. Ninety-five per cent of the controls and 96% of the drug group completed 12 months of observation, and 91% and 92% respectively, 18 months. At the longer durations of 36 or 48 months, the controls slightly outlasted those given drugs. It should be pointed out that, while all the patients had an opportunity to be followed up for two years, only those enrolled during the earlier periods of the study could have been observed for three to six years. Thus the low percentages seen after 24 months reflect mainly a later date of enrolment and not lack of co-operation.

X-ray and Sputum Examinations

As time passed, particularly after discontinuation of the drugs, the intervals between visits increased, so that the overall frequency of x-ray examinations was one for every 6.3 person-months in the controls and one for every 5.3 person-months in those taking drugs; one sputum examination was done for every 11.2 person-months in the controls and one for every 11.7 person-months in those taking drugs.

TABLE III.—Side Effects Attributed to Chemoprophylaxis
Initially placed on INH alone (879)* INH+PAS (657)*

		INH		*PAS*	
		No.	*%*	*No.*	*%*
Symptoms leading to discontinuation of one or both drugs	Gastrointestinal	47	5.3	187	28.9
	CNS	48	5.6	31	4.8
	"Neuropathy"	26	3.0	6	0.9
	Hypersensitivity	28	3.3	28	4.3
	Other	15	1.7	21	3.3
Subtotal		164	18.9	273	42.2
Symptoms not leading to discontinuation of one or both drugs	Gastrointestinal	25	2.9	97	14.9
	CNS	31	3.6	17	2.6
	"Neuropathy"	15	1.7	2	0.4
	Hypersensitivity	14	1.6	1	0.2
	Other	19	2.2	10	1.5
Subtotal		104	12.0	127	19.6
No symptoms		598	69.1	247	38.2
Total		866	100.0	647	100.0

* Includes 13 patients initially placed on INH and 10 patients started on INH+PAS who have no record relating to side effects.

Side Effects

The incidence of symptoms ascribed by patients to medication is shown in Table III. According to these figures, nearly one-third of those on INH alone and nearly two-thirds of those on INH plus PAS complained of such symptoms. In nearly 20% of those on INH alone and in over 40% of those on INH plus PAS the symptoms led to discontinuation of one or both drugs. Gastrointestinal symptoms were predominant in the INH-plus-PAS group, accounting for discontinuation of the drugs in nearly 30% of the patients. In the group on INH alone, these symptoms caused discontinuation in about 5%. Indigestion and diarrhea were the most common gastrointestinal symptoms. Central nervous system symptoms, such as dizziness and drowsiness, caused discontinuation of the drugs in about 5% of both groups. The symptoms suggestive of "neuropathy", e.g. tingling and numbness in the extremities, required stopping the drug in about 3% of those on INH and in about 1% of those on INH plus PAS. Symptoms suggestive of hypersensitivity, including various skin rashes and fever,

caused discontinuation of the drugs in 3 to 4% of both groups. A few other symptoms, such as weight gain, discolouration of teeth, impotence and dyspnea, occurred in both groups, accounting for discontinuation in 2 to 3%.

Duration of Drug Administration

Table IV shows the duration of the administration of the drugs. Of the 657 who were originally allocated to INH plus PAS, 221 had stopped taking PAS but continued with INH alone; 138 of these took PAS for less than four months (average: 28 days) and are included with those taking INH alone, while 83 who took PAS for more than four months (average: nine months) are considered with the INH-plus-PAS group. The dropouts in taking drugs exceed the dropouts in attendance. Of all those taking drugs, 82% claimed to have completed three months, 74% six months and 64% one year. Some took their drugs for a longer period. The group taking INH plus PAS suffered slightly greater losses than those taking INH alone. These figures require qualification. When urine tests (Phenistix for PAS and Eidus' test for INH) were done repeatedly on patients in one clinic (Willow, Vancouver), about 60% were consistently positive, 25 to 30% were shown to be irregular and 5 to 10% were consistently negative. Therefore, in all probability, some patients took the drugs in lesser amount and less continuously than the figures in Table IV might suggest.

REACTIVATIONS*

In Controls

The reactivations in the controls in relationship to the amount of risk-experience (as expressed in person-months) are shown in Table V. The frequency in groups I and III is slightly lower than in group II. All controls combined had a total risk-experience of 34,443 person-months with 14 reactivations—a rate of 40.6 per 100,000 person-months or 4.9 per thousand persons per annum. The differences between the occurrence of reactivations in the different periods well illustrate the play of chance alone in the figures.

While Taking Drugs

Reactivations occurring during the administration of the drugs are shown in Table VI. There was only one reactivation in a risk-experience of 17,461 person-months, when, according to the rates in the controls, about seven might have been expected in the absence of chemoprophylaxis. This reactivation occurred among those taking INH alone in the fourth month of treatment. There were no reactivations during the later stages of INH therapy and none in the patients taking the INH plus PAS.

After Stopping Drugs

The reactivations during the period after the drugs were stopped are shown in detail in Table VII and summarized in Table VIII. There were nine reactivations in the 42,606 person-months of observation—a rate of 21.1 per 100,000. Of the nine reactivations, six occurred in persons who took drugs for less than six months; of those who took drugs for more than six months, three reactivations occurred in those taking INH alone and none in the INH-plus-PAS group.

The short treatment of under six months' duration apparently failed to protect against reactivation. The annual rate in this group was 5.1 per thousand, similar to that seen in controls (4.9 per thousand). In those taking longer courses of treatment the reactivation rate was 1.9 per thousand for the group on INH alone; no reactivation occurred in the INH-plus-PAS group (Table VII).

In all patients who took drugs for more than six months (INH alone or INH plus PAS) there were three cases (in a risk-experience of 28,615 person-months); according to the rates in controls, 12 cases might have been expected.

Resistance

In the chemoprophylaxis group resistance to INH was observed in the bacilli isolated from two of the patients with reactivations; both received a course of INH alone for 12 months. It is not known whether the resistance in the two cases was

TABLE V.—Reactivations in Controls (No Chemoprophylaxis)

Period of observation	*Groups I and III (486)* P.M.*	Rctns.†	*Group II (354)* P.M.	Rctns.	*Total (840)* P.M.	Rctns.
1st year	5656	3	4034	1	9690	4
2nd year	5328	1	3886	2	9214	3
3rd year	3948	—	3666	1	7614	1
4th year	1792	2	3157	4	4949	6
5th and subsequent years	670	—	2306	—	2976	—
Total	17394	6	17049	8	34443	14
Reactivations — Per 100,000 person months	34.5		46.9		40.6	
Rate — Annual rate per 1000	4.1		5.6		4.9	

* Person-months † Reactivations

TABLE VI.—Reactivations While Taking Drugs

Period of taking drugs	*INH alone (1017)* P.M.*	Rctns.†	*INH & PAS (519)* P.M.	Rctns.	*TOTAL (1536)* P.M.	Rctns.
1st 3 months	2668	—	1316	—	3984	—
2nd 3 months	2362	1	1142	—	3504	1
2nd 6 months	4187	—	2061	—	6248	—
3rd 6 months	1615	—	1544	—	3159	—
4th 6 months	179	—	212	—	391	—
3rd year	40	—	55	—	95	—
4th year	35	—	45	—	80	—
Total	11086	1	6375	—	17461	1
Reactivation rate — per 100,000 person months	9.0		0		5.7	
Reactivation rate — Annual rate per 1000	1.1		0		0.7	

* Person-months † Reactivations

*A table which sets forth the details of individual reactivations can be obtained from the senior author.

present previously or developed as a result of administration of the drug. In five other reactivations following chemoprophylaxis the bacilli were found to be sensitive to INH. Sensitivity studies were done in nine of the control group; eight were sensitive to INH, PAS and streptomycin and one was resistant to streptomycin and PAS but sensitive to INH.

Deaths

Deaths in the controls numbered 24, one being charged to tuberculosis. In those given drugs, there were 40 deaths, none of which was charged to tuberculosis.

DISCUSSION

This is a study of 2376 patients with inactive pulmonary tuberculosis who attended 30 clinics in five Canadian provinces. Eighty-eight per cent of these patients had not received any previous antimicrobial treatment; the remainder received drugs for a period of less than three months. These cases were divided into two main groups: those given drugs (INH plus PAS or INH alone) and those enrolled as controls. The controls consisted of those to whom chemoprophylaxis was not offered and those who refused it. These groups were found to be quite comparable in so far as various factors of possible prognostic significance are concerned, such as age and sex, previous bacteriological findings, extent of disease and duration of inactive interval.

This study showed that patients taking chemoprophylaxis were to a considerable extent protected against the danger of reactivation during the time they were on drugs, and those who took the longer course of drugs were similarly protected during the subsequent period of observation. The reactivation rate in all patients taking antimicrobial drugs was 0.7 per 1000 per year during the period of treatment and remained at a comparable low level (1.3 per 1000 per year) in those who took treatment for more than six months. In contrast, patients who took a course of chemoprophylaxis for less than six months suffered, during the subsequent period, a reactivation rate of 5.1 per 1000 per year. The reactivation rates in the two control groups were 4.1 and 5.6 per 1000 per year.

The occurrence of only one reactivation while taking the drugs when, according to the rate in the controls, about seven might have been expected, leaves no doubt, in spite of the small numbers, that the drugs, while being taken, greatly reduced the number of reactivations.

Three reactivations occurred in the groups which had taken drugs for over six months, whereas about 12 could have been expected, demonstrating the sustained effectiveness of chemoprophylaxis. As the risk of reactivation in inactive cases of tuberculosis of long standing remains fairly constant, there is every expectation that patients who took medication for an adequate period will continue to show a low reactivation rate. Although the play of chance could readily account for the absence of any reactivations after a longer course of combined administration of INH plus PAS, the conformity with clinical experience in the treatment of active tuberculosis strongly supports the suggestion that the elimination of reactivations was attributable to this regimen.

Thus, though the numbers in this trial are too small and its duration is too short to provide a solid basis for a *precise estimate* of the efficacy of chemoprophylaxis, the results (when considered along with clinical experience) show that chemoprophylaxis for less than six months is insufficient but that longer periods of chemoprophylaxis are highly effective in preventing reactivations, and that PAS in addition to INH is probably superior to INH alone.

The fact that chemoprophylaxis of previously untreated inactive cases of tuberculosis is effective has been shown in the studies conducted by the United States Public Health Service where, by the administration of INH alone for 12 months, morbidity was reduced by 64%.[2]

All of the bacteriologically confirmed reactivations occurring after short courses of chemoprophylaxis showed sensitivity to isoniazid. Of the three reactivations in patients taking INH for over six months,

TABLE VIII.—Reactivations in Treatment Groups After Stopping Drugs

Duration of treatment		*Under 6 months*		*Over 6 months*	
		INH alone	*INH+PAS*	*INH alone*	*INH+PAS*
Person-months		8300	5691	18482	10133
No. of reactivations		4	2	3	0
Reactivation rate	Per 100,000 person-months	48.2	35.1	16.2	—
	Annual rate per 1000	5.8	4.2	1.9	—
		5.1		1.3	

TABLE VII.—Reactivations After Stopping Drugs

Chemoprophylaxis	*Period of taking drugs (as stated)*	*1st year* P.M.*	Rctn.†	*2nd year* P.M.	Rctn.	*3rd year* P.M.	Rctn.	*4th year* P.M.	Rctn.	*5th year* P.M.	Rctn.	*6th year* P.M.	Rctn.	*TOTAL* P.M.	Rctn.	*Rate/ 100,000**		*Rate/ 1000‡*	
INH	0-2 mos.	2079	2	1717	—	1278	—	508	—	148	—	58	—	5788	2	34.5	48.2	4.15	5.8
	3-5 mos.	1106	1	663	—	427	—	197	1	90	—	29	—	2512	2	79.6		9.56	
	6-11 mos.	1084	—	780	—	405	—	140	—	31	—	7	—	2447	—	—	16.2	—	1.9
	12-17 mos.	4547	1	3940	1	2344	—	786	1	161	—	13	—	11791	3	25.4		3.05	
	18-23 mos.	2081	—	1309	—	571	—	249	—	34	—	—	—	4244	—	—		—	
	Sub-total	10897	4	8409	1	5025	—	1880	2	464	—	107	—	26782	7	26.1		3.14	
INH plus PAS	0-2 mos.	1352	—	1170	2	1163	—	581	—	—	—	—	—	4266	2	46.9	35.1	5.63	4.2
	3-5 mos.	520		340		257		176		115		17		1425		—		—	
	6-11 mos.	472		341		278		128		65		—		1284		—	—	—	0
	12-17 mos.	958		861		516		211		69		—		2615		—		—	
	18-23 mos.	2249		1833		1298		742		112		—		6234		—		—	
	Sub-total	5551	—	4545	2	3512	—	1838	—	361	—	17	—	15824	2	12.6		1.5	
	Total	16448	4	12954	3	8537	—	3718	2	825	—	124	—	42606	9	21.1		2.5	

* Person-months † Reactivations ‡ Per annum

two (treated for 12 months and 14 months, respectively) showed resistance to INH, while the bacilli in the third (treated for 12 months) were found to be sensitive. It is probable that INH chemoprophylaxis led to the development of resistance in the two cases. On the other hand, it is possible that the bacilli were originally resistant to INH.

The unexpected and disappointing finding in this trial was the relatively large number of patients who discontinued treatment prematurely; 25.7% of those placed on chemoprophylaxis discontinued the drugs within the initial six-month period of what was to be at least one year of therapy. Furthermore, urine tests for PAS and INH derivatives performed in one of the clinics showed that about 5 to 10% of patients who stated that they took their drugs probably did not do so. The greater dropout rate in those taking INH plus PAS than in those taking INH alone was due largely to the gastrointestinal side effects of PAS. While the loss in those taking drugs is disappointing, it is not surprising. Allen, Stewart and Jeney,[3] in an intensive survey of post-sanatorium chemotherapy of ambulatory cases of active tuberculosis under relatively close clinic supervision, found that only about 50% of patients took their drugs regularly or in the prescribed amount. It could hardly be expected that our group would show a perfect record of regularity and persistence in taking their pills. These findings should not be taken at their face value, as many of the patients took their treatment believing that they did so as part of a research project rather than for their own benefit. There is no doubt, however, that chemoprophylaxis, if it is to be successful, requires not only strong motivation in the patient engendered by an enthusiastic physician, but also adequate supervision. In certain situations closely supervised regimens of chemoprophylaxis may prove possible.

The main reason for discontinuation of treatment was the occurrence of real or imaginary side effects from drugs. The much higher frequency of side effects in this trial than that experienced in the chemotherapy of active tuberculosis is not satisfactorily explained. Certainly the participants were particularly questioned regarding side effects, and this may have increased the tendency to complain. A much higher frequency of gastrointestinal side effects in the group taking INH plus PAS than in those taking INH alone is similar in direction to, but much greater in extent than, that found in the chemotherapy of active tuberculosis. The lesser frequency of disturbing neuropsychiatric symptoms in those taking INH plus PAS (0.9%) than in those taking INH alone (3.0%) may be due to chance. The fact that of the small group (18) on placebo, five (28%) developed side effects indicates that many of the complaints in the group taking drugs might well have been of a similar nature. No serious life-threatening complications from taking the drugs were encountered in this experience. Ferebee,[4] in the United States Public Health Service chemoprophylaxis trials with INH alone, had a much happier experience, as only 3% had side effects.

As in a former survey,[1] the reactivations observed in this project are much fewer than is reported by others. For instance, Katz *et al.*[5] reported rates several times those found here. The difference is attributable, it is thought, to a difference in selection of the inactive cases. Eighty-six per cent of those allocated to drugs and 92% of the controls in this study had an inactive status of more than 10 years' duration, by which time the rate of reactivation is only a fraction of that in the first few years. The rate in the controls, 4.9 per 1000 persons per annum, corresponds closely with that found previously in the cases with a long inactive period.[5]

The mechanism of the action of chemoprophylaxis is not quite clear, but presumably it acts by diminishing bacterial population in the lesions. Theoretical arguments advanced against chemoprophylaxis in inactive tuberculosis have been of two kinds. Firstly, because the bacilli in these lesions are dormant, and as antimicrobial drugs act only on multiplying bacteria, it was argued that the drugs could not be effective. Secondly, the bacilli were thought to be walled-off and therefore inaccessible to drugs. As chemoprophylaxis obviously exerts a profound influence on the course of inactive tuberculosis, these arguments are not applicable. Possibly our concept of inactive disease, which we often equate with the healed, burned-out process, is wrong. It seems more likely that many "inactive" cases show in reality a continuous low-grade activity in which a precarious balance is struck between the host and a rather large bacterial population; this degree of activity is so low that it is difficult to discover by current diagnostic methods.

Other studies, as well as a further follow-up of the patients enrolled in this trial, will delineate the type and duration of effective courses of chemoprophylaxis. At present, with rather scanty knowledge, it seems wise to consider that the principles applicable to the treatment of active tuberculosis will likely prove applicable to the chemoprophylaxis of inactive cases. In these patients with probably a large bacterial population, we believe that it is generally preferable to start with the two-drug regimen and to change over to treatment with INH alone if and when side effects become apparent. Further investigations on the effectiveness of more intensive as well as of completely supervised regimens are needed.

In general two philosophies are emerging relating to the use of chemoprophylaxis in the control of tuberculosis. Some would use it very widely in large groups of the population, that is, in all positive reactors. Others would restrict its use to the relatively small number

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of individuals with a particularly high risk of developing active tuberculosis. We are in favour of this second approach, as we believe that more will be accomplished by giving chemoprophylaxis to relatively small, high-risk groups with the possibility of thorough motivation and supervision, than by its use in both high- and low-risk situations which inevitably results in rather haphazard performance.

Reactivations contribute about one-quarter to one-third of all active cases in Canada[6] and, in addition, constitute the reservoir from which other cases arise. Yet persons with inactive tuberculosis form only 1.0 to 1.5% of the population.

Chemoprophylaxis given to inactive cases of tuberculosis previously untreated with antimicrobial drugs is effective in preventing reactivations; the widespread and diligent application of this measure will result in a marked reduction of tuberculosis morbidity and should be considered one of the high priorities in the tuberculosis control program.

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Résumé

Essai de chimioprophylaxie de la tuberculose inactive au canada

A 1536 sujets atteints de tuberculose latente, on a appliqué un traitement préventif comportant soit l'isoniazide (INH) seul, soit l'INH et l'acide paraminosalicylique (PAS) associés. Ont servi de témoins 840 cas semblables. L'abandon du traitement a été fréquent généralement à cause de malaises que les malades attribuaient aux médicaments qu'ils prenaient.

La proportion annuelle de réactivation a été de 4.9 par 1000 chez les témoins. Pendant la période de médication, le groupe traité a montré une proportion annuelle de réactivation de 0.7 par 1000. Ceux qui avaient pris la médication pendant au moins six mois présentèrent un taux de réactivation annuelle de 1.3 par 1000. Le taux chez ceux qui avaient abandonné le traitement pendant les six premiers mois a été de 5.1 par 1000. On n'a pas constaté d'épisode de réactivation chez les malades qui ont pris l'INH et le PAS pendant plus de six mois. On a également noté une résistance du bacille à l'INH dans deux cas de réactivation qui avaient été traités à l'INH seule pendant une longue période.

La chimioprophylaxie des cas de tuberculose inactive est une arme puissante pour éliminer la maladie. Il faut cependant y recourir à bon escient et surveiller les malades.

This was a co-operative study and our grateful thanks are due to the directors of tuberculosis control in Ontario, Saskatchewan, Quebec, Alberta and British Columbia, and to the following physicians and their staffs who participated in this study: Dr. W. J. Downs, Edmonton, Alta.; Drs. W. W. Middleton and M. M. Mosbaugh, London, Ont.; Dr. J. S. Hazen, Brantford, Ont.; Dr. C. L. Law, Sardis, B.C.; Drs. J. B. Cook and C. J. Doherty, Sudbury, Ont.; Dr. N. M. Beattie, Hamilton, Ont.; Drs. D. R. Brown and W. Pile, Windsor, Ont.; Dr. S. J. Hawkins, Kitchener, Ont.; Drs. H. T. McClintock and E. P. Snider, Toronto, Ont.; Dr. E. R. Harris, Kirkland Lake, Ont.; Dr. E. A. Allen, Lindsay and Peterborough, Ont.; Dr. W. D. Wigle, Toronto, Ont.; Dr. C. R. Weber, Windsor, Ont.; Dr. G. J. L. Davies, Ottawa, Ont.; Drs. M. L. Allan and A. Hakstian, New Westminster, B.C.; Drs. A. Scott and F. Dubsky, Fort William, Ont.; Drs. C. G. Shaver and W. M. McGregor, St. Catharines, Ont.; Dr. J. L. Naismith, Kingston, Ont.; Dr. H. J. Irwin, Orillia, Ont.; Dr. G. Lane, Hearst, Ont.; Dr. J. Baltrusaitis, North Bay, Ont.; Drs. G. G. Brearley and A. C. McKenna, Belleville, Ont.; Dr. M. A. Hickey, Montreal, Que.; Dr. A. G. Jessamine, Ottawa, Ont.; Dr. M. Barry, Regina Sask.; Dr. Z. Gorecki, Cornwall, Ont.; Dr. J. F. Paterson, Toronto, Ont.; Dr. R. M. Lane, Victoria, B.C.; and Dr. F. D. MacKenzie, Vancouver, B.C.

We would like to express our appreciation to the staff of the Division of Tuberculosis Prevention of the Department of Health of Ontario, and particularly to Dr. Laila Tuters and Mrs. Sheila Johnson who have assisted greatly in the initial stages of this study.

The late Mr. Paul Donaldson, a medical student at the University of British Columbia, was most helpful in compiling some of the data.